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(54) Title: MODIFIED CD8 MOLECULE, NUCLEIC ACID ENCODING SAID MOLECULE, AND THEIR THERAPEUT IC USE

(57) Abstract: The present invention provides modified CD8 molecules whose binding to MHC is enhanced compared to wild type CD8, wherein Ser₅₃ of at least one CD8α chain thereof is mutated to another amino acid. It also provides nucleic acids encoding such molecules, and to the use of such molecules and nucleic acids in immunosuppressive therapy, in particular as inhibitors of cytotoxic T cell responses.

INTERNATIONAL SEARCH REPORT

Internation Application No
PCT/GB 02/02743

| IPC 7 | SIFICATION OF SUBJECT MATTER C07K14/705 C12N15/12 C1 | 0111 / 70 | | C1/6B 02/02743 | |
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| A | WO 99 21576 A (GERTH ULRICH ;JAKOBSEN BENT KARSTEN (GB); (GB) 6 May 1999 (1999-05-06) the whole document | 1-21 | | | |
| A | molecular basis for function coordination with the T-cell IMMUNOLOGY TODAY, ELSEVIER PLANBRIDGE, GB, vol. 21, no. 12. | MUNOLOGY TODAY, ELSEVIER PUBLICATIONS, IMBRIDGE, GB, IMBRI | | | |
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| | r documents are listed in the continuation of box C. | ΧF | atent family member | s are listed in annex. | |
| Special categories of clied documents: document defining the general state of the art which is not considered to be of particular relevance earlier document but published on or after the international filing date document which may throw doubts on priority claim(s) or which is clied to establish the publication date of another cliation or other special reason (as specified) document referring to an oral disclosure, use, exhibition or other means document published prior to the international filing date but later than the priority date claimed | | cited invention of the color of | 'T' later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention. 'X' document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone or document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. '&' document member of the same patent family | | |
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| ne and mail | ing address of the ISA | Authori | zed officer | | |
| | European Patent Office, P.B. 5818 Patentlean 2 NL ~ 2280 HV Rijswijk Tel: (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016 | | echner, O | | |

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| C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT | | | | | | |
| Category ° | the elevent propaga | Relevant to claim No. | | | | |
| A | SEWELL A K ET AL: "Antagonism of cytotoxic T-lymphocyte activation by soluble CD8." NATURE MEDICINE. UNITED STATES APR 1999, vol. 5, no. 4, April 1999 (1999-04), pages 399-404, XP002255511 ISSN: 1078-8956 the whole document | 1-21 | | | | |
| А | KERN P S ET AL: "Structural basis of CD8 coreceptor function revealed by crystallographic analysis of a murine CD8alphaalpha ectodomain fragment in complex with H-2Kb." IMMUNITY. UNITED STATES OCT 1998, vol. 9, no. 4, October 1998 (1998-10), pages 519-530, XP002255512 ISSN: 1074-7613 the whole document | 1-21 | | | | |
| A | LI S ET AL: "Identification of the CD8 DE loop as a surface functional epitope. Implications for major histocompatibility complex class I binding and CD8 inhibitor design." THE JOURNAL OF BIOLOGICAL CHEMISTRY. UNITED STATES 26 JUN 1998, vol. 273, no. 26, 26 June 1998 (1998-06-26), pages 16442-16445, XP002255513 ISSN: 0021-9258 the whole document | 1-21 | | | | |

INTERNATIONAL SEARCH REPORT

International application No. PCT/GB 02/02743

| Box I | Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of Iirst sheet) | | | | | |
|------------|--|---|--|--|--|--|
| This Int | emational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons: | - | | | | |
| 1. X | Claims Nos.; because they relate to subject matter not required to be searched by this Authority, namely: | | | | | |
| | Although claims 19 (only as far as relating to an in vivo method) and 20 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition. | | | | | |
| 2 | Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful international Search can be carried out, specifically: | | | | | |
| . — | | | | | | |
| 3 | Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a). | | | | | |
| Box II | Observations where unity of invention is lacking (Continuation of item 2 of first sheet) | + | | | | |
| This Inter | rnational Searching Authority found multiple Inventions in this international application, as follows: | 1 | | | | |
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| 1 | As all required additional search fees were timely paid by the applicant, this international Search Report covers all searchable claims. | | | | | |
| 2 | As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee. | | | | | |
| з | as only some of the required additional search fees were timely paid by the applicant, this international Search Report overs only those claims for which fees were paid, specifically claims Nos.: | | | | | |
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| 4. N | to required additional search fees were timely paid by the applicant. Consequently, this international Search Report is estricted to the invention first mentioned in the claims; it is covered by claims Nos.: | | | | | |
| | \cdot | | | | | |
| Remark or | Protest The additional search fees were accompanied by the applicant's protest. | | | | | |
| | No protest accompanied the payment of additional search fees. | | | | | |
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INTERNATIONAL SEARCH REPORT

Information on patent family members

PCT/GB 02/02743

| | | | | D. d. Handley |
|--|------------------|---|--|--|
| Patent document cited in search report | Publication date | Patent fami member(s | | Publication date |
| WO 9921576 A | 06-05-1999 | CN 12831 DE 698048 DE 698048 DK 10248 EP 10248 ES 21757 WO 9921! HK 10310 JP 20015210 NO 20002: NZ 5047 | 10 B2 98 A 63 A1 20 T 39 D1 39 T2 322 T3 322 A1 798 T3 576 A1 999 A1 | 15-04-2002 03-10-2002 17-05-1999 06-05-1999 07-02-2001 16-05-2002 10-10-2002 05-08-2002 09-08-2000 16-11-2002 06-05-1999 13-12-2002 06-11-2001 27-06-2000 26-11-2002 30-09-2002 |

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